DECLARATION

1. I, Robert Gordon Hood, hereby declare as follows.

2. I am a co-inventor of US patent application serial no. 10/597,677. My Curriculum Vitae is annexed to this declaration.

3. I have been responsible for a series of experiments comparing drug elution from a coated, standard stent with elution from a coated stent with a spiral inducer. I will now explain the experiments conducted and the results of the experiments in detail.

4. Preliminary investigations were carried out in order to determine a suitable coating mixture for the stents, as set out in Annex A. In these experiments, Aspirin was selected as the drug for elution. From these investigations, it was concluded that polyurethane could be successfully diluted with tolulene to form less viscous solutions, suitable for dip coating stents and still cure. The optimum dilution of polyurethane for dip coating was obtained by mixing 1 part PU with 2 parts toluene. Asprin could be successfully incorporated into the PU mixture and released at a measurable rate over time.

5. The control stents and the spiral stents were tested in a flow rig as described in Annex B. In brief, water was passed through each stent and the run off water collected in a collection tank. Samples from the collection tanks were taken and analysed on a spectrophotometer to determine the absorption of the drug into the water. The rate of water flow and the mass of Aspirin coated on the stents was varied over four different runs.

6. A summary of the results from all four runs is shown below.

Data Obtained from the Collection Tank

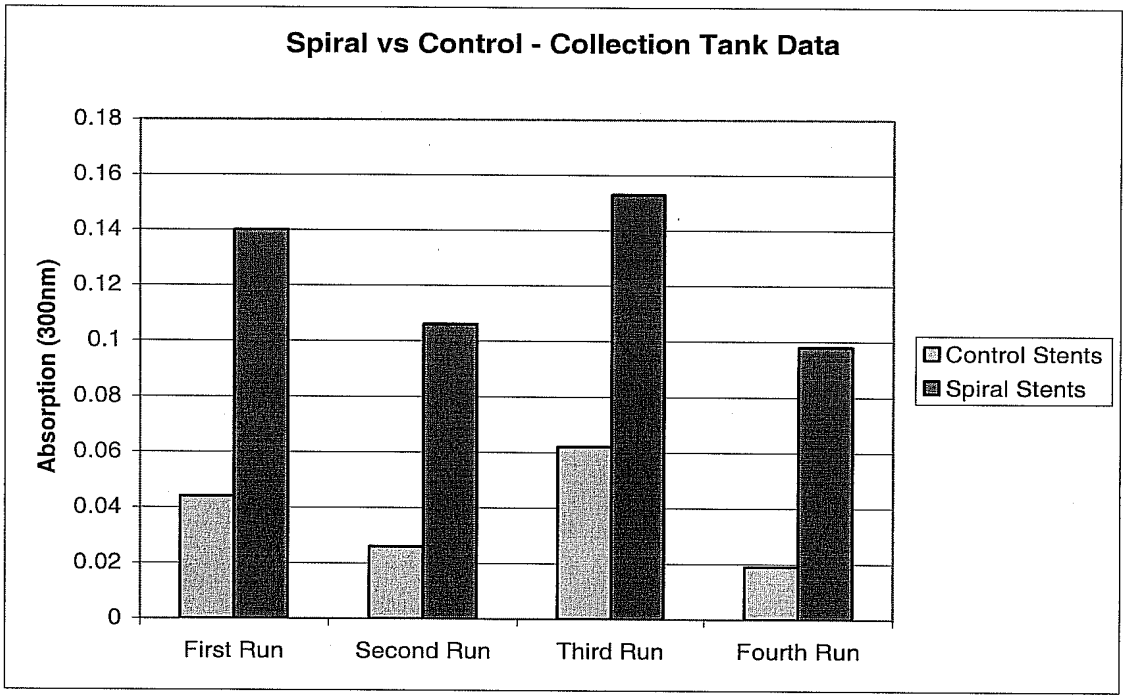
Total Load of Aspirin Present in the Coating of Each Stent

	Total Aspirin Present in Coatings (g)		Increase of Aspirin Load on Spiral Stent
	Control	Spiral	
First Run	0.0176	0.039	55.5%
Second Run	0.0148	0.037	60%
Third Run	0.0148	0.037	60%
Fourth Run	0.0074	0.0148	50%

Absorption of Aspirin Present in the Collection Tank After Every Run

	Absorption of Aspirin (300nm)		Increase in Absorption from Spiral Stent
	Control	Spiral	
First Run	0.044	0.140	69%
Second Run	0.026	0.106	75%
Third Run	0.062	0.153	59%
Fourth Run	0.019	0.098	81%

The results are shown graphically as follows.



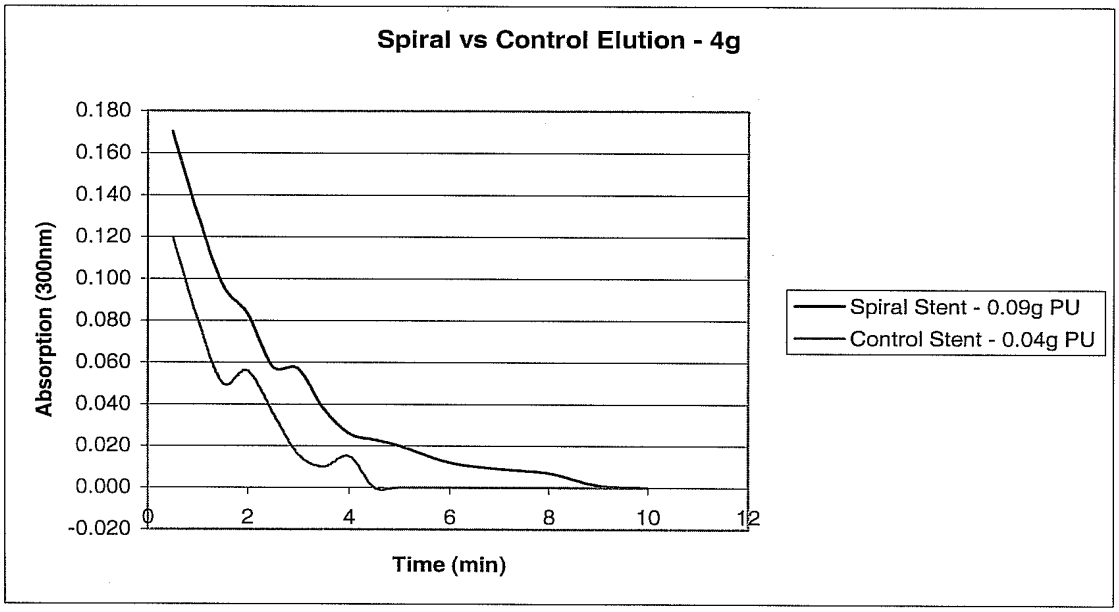
Aspirin Eluted in Comparison to Load

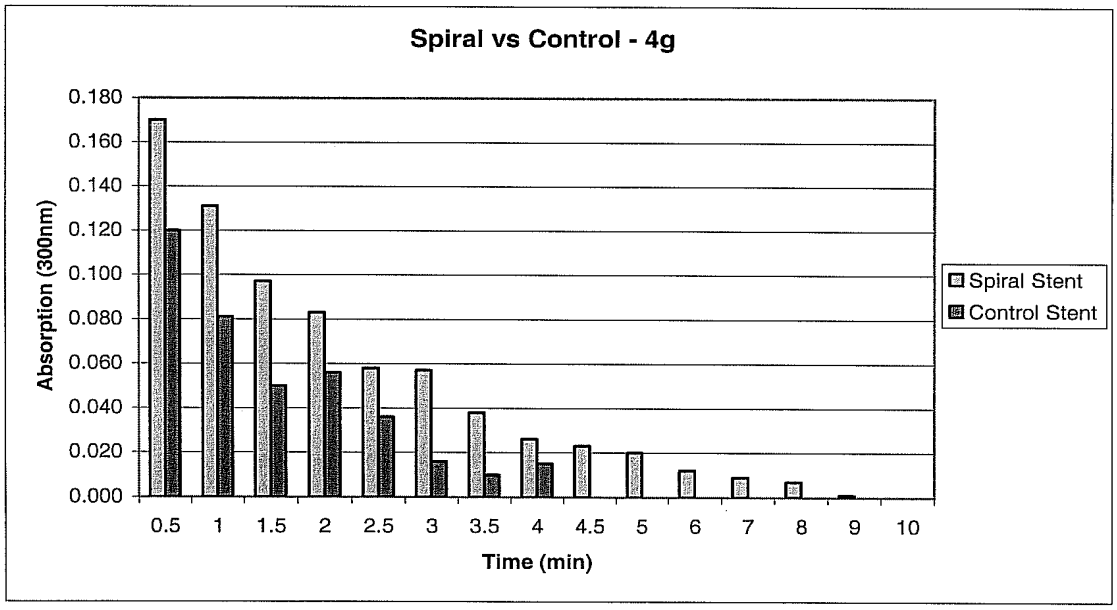
	First Run		Second Run		Third Run		Fourth Run	
	Control	Spiral	Control	Spiral	Control	Spiral	Control	Spiral
Aspirin on Stent (μg)	17.6	39	14.8	37	14.8	37	7.4	14.8
Aspirin Eluted (μg)	1.55	496	0.21	210	2.86	396	0.348	174

Tables showing actual absorption are provided in Appendix 2

7. The detailed results of the first run are shown below.

First Run – 4g Aspirin, 310 ml/min





8. **First Run of Control vs Spiral Stents**

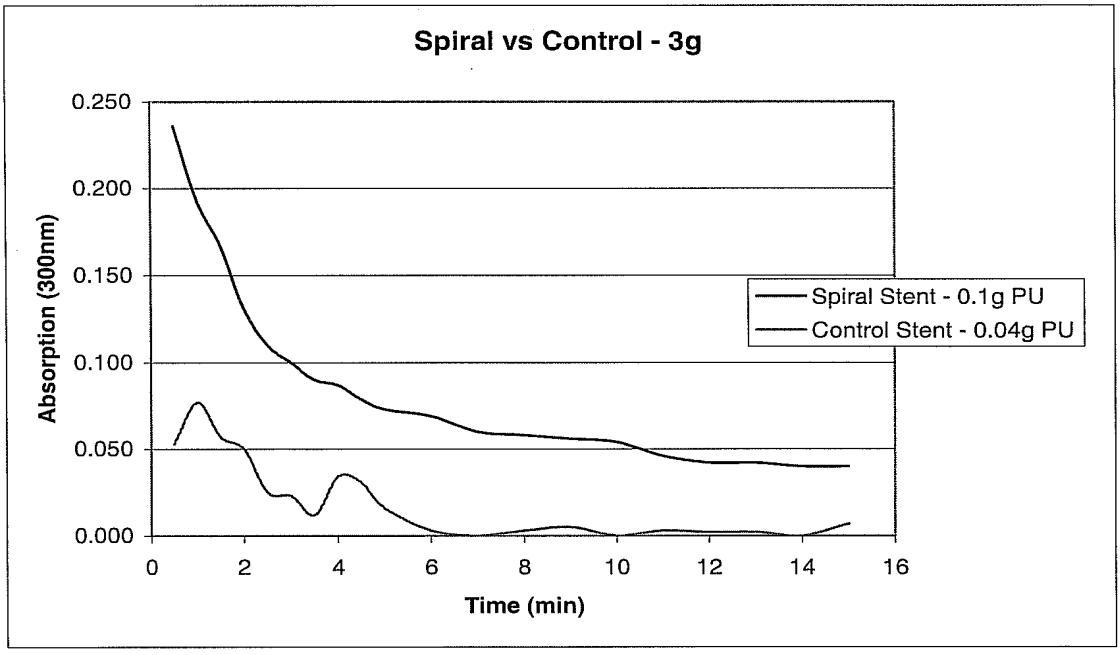
The weight of the stents, measured before and after coating, show that the spiral stent has a 55.5% greater coating load than the control stent.

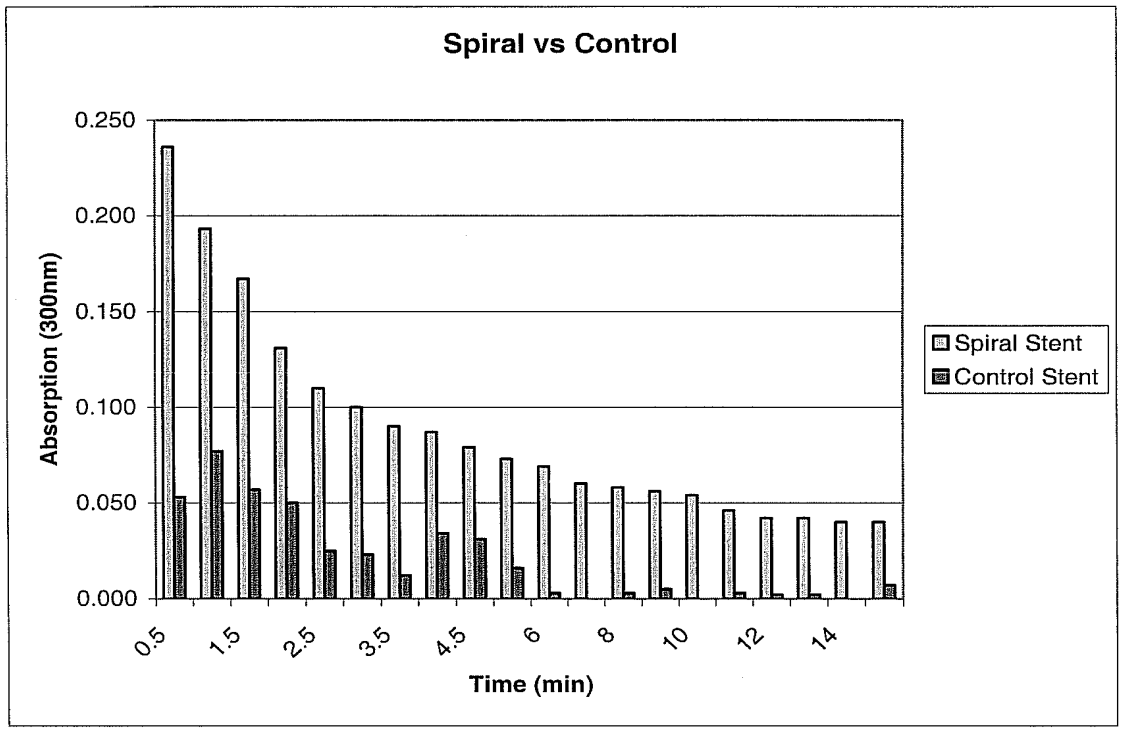
The spiral stent eluted 65% more aspirin than the control stent over 10min (value obtained by averaging the absorbtion figures over that time period). The control stent ceased eluting aspirin after 4min. The spiral stent continued releasing the drug for 9min.

After the testing in the flow rig, the stents were soaked overnight in 100ml Distilled water and then absorption was measured. This showed that high doses of aspirin had been released from the coating on the stents suggesting that perhaps elution had not stopped completely but slowed down to a level that could not be detected in a 20 min test.

9. The detailed results of the second run are shown below

Second Run – 3g Aspirin, 280ml/min



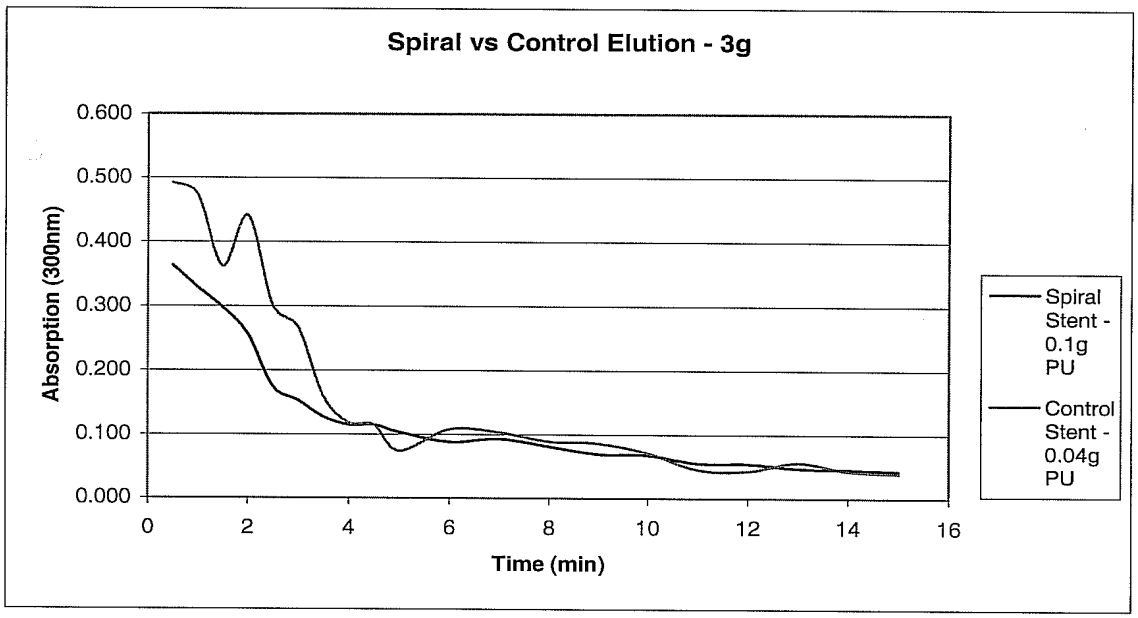


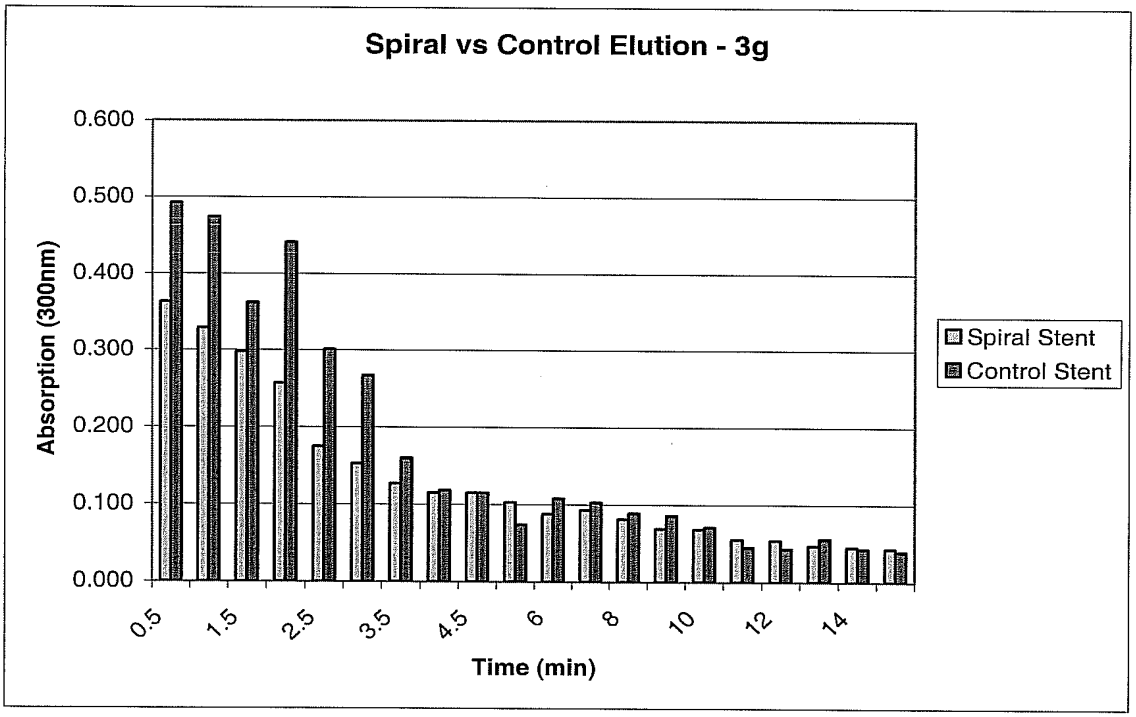
10. Second Run of Control vs Spiral

In this test the concentration of aspirin was reduced from 4g to 3g in order to ascertain whether the result could be replicated at different levels. The coating on the spiral stent was 60% heavier than that on the control and the results of the flow test show that the spiral stent eluted 82.7% more aspirin than the control. This increase is considerably higher than the 65% increase shown in the first run, it is possible that the increase was falsely elevated due to the spiral stent having been re-coated. In order to try and reduce this effect stents were washed thoroughly in IPA and water to try and remove all the aspirin from the coating.

11. The detailed results of the third run are shown below.

Third Run – 3g Aspirin, 295ml/min





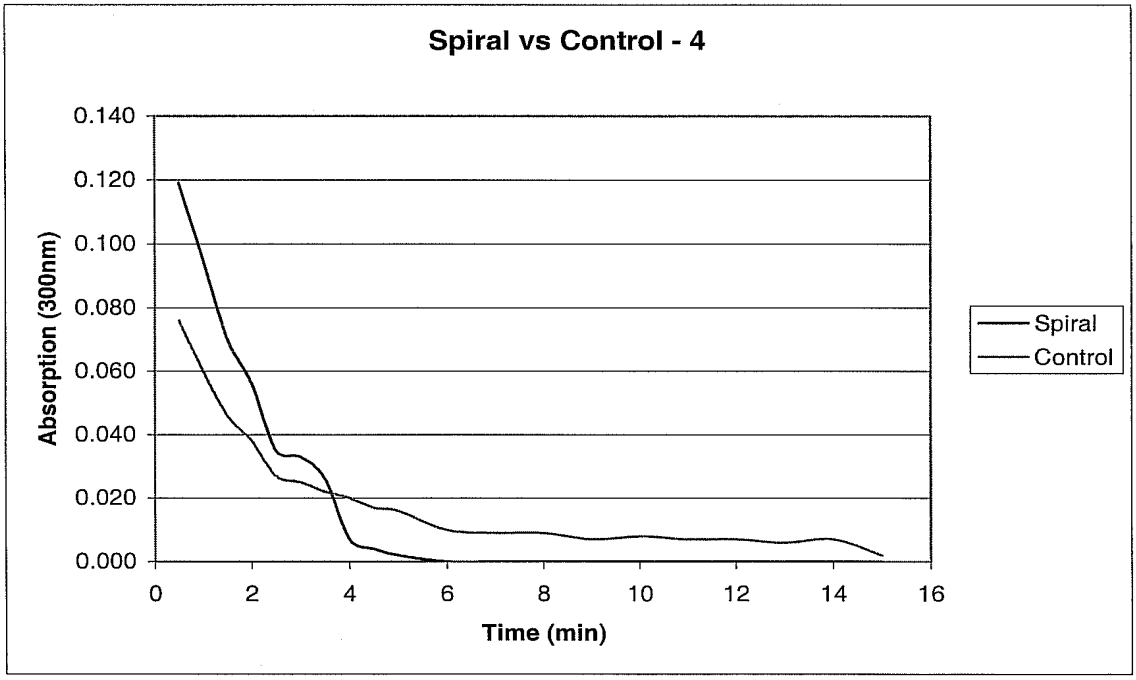
12. **Third Run of Control vs Spiral**

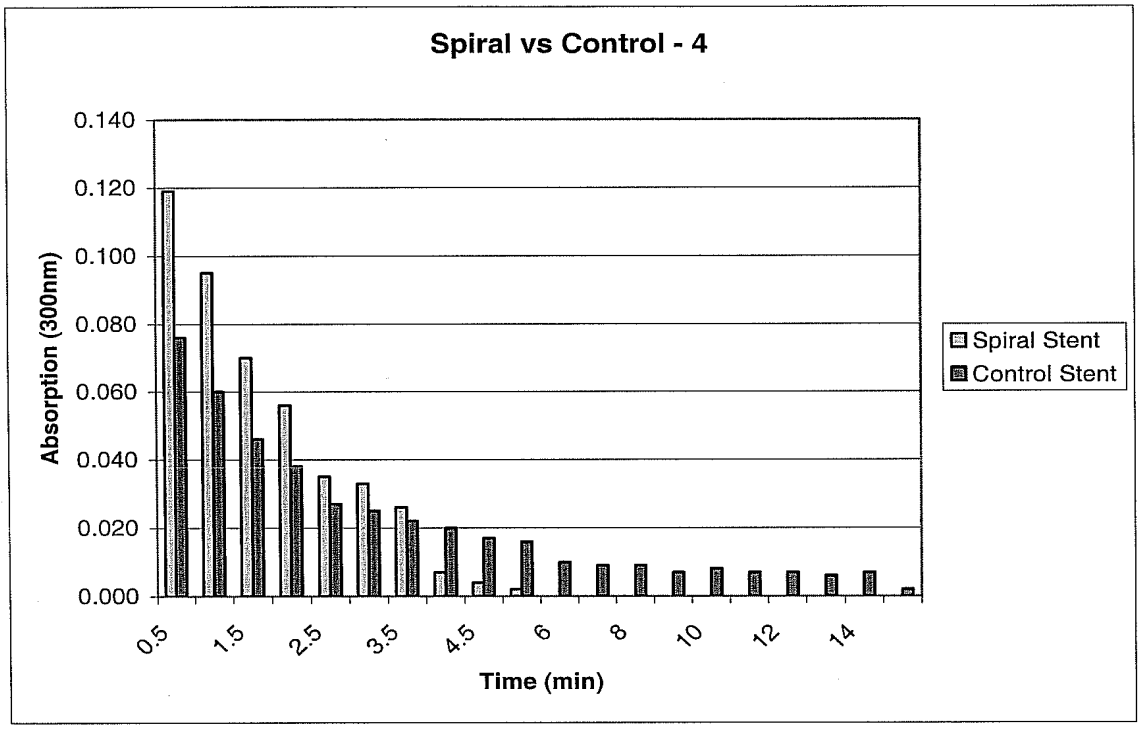
The results obtained from the samples taken at the injection port show almost a total reversal to those obtained in previous experiments. The control stent released 17.9% more aspirin than the spiral despite the spiral having a 60% heavier coating. This anomaly was probably due to a contaminated blank in the spectrophotometer as the sample taken from the collection tank at the completion of the study showed an increased absorbance of 59% in the spiral group.

13. The detailed results of the fourth run are shown below.

Fourth Run – 3g Aspirin, 290ml/min

Sample from Injection Port





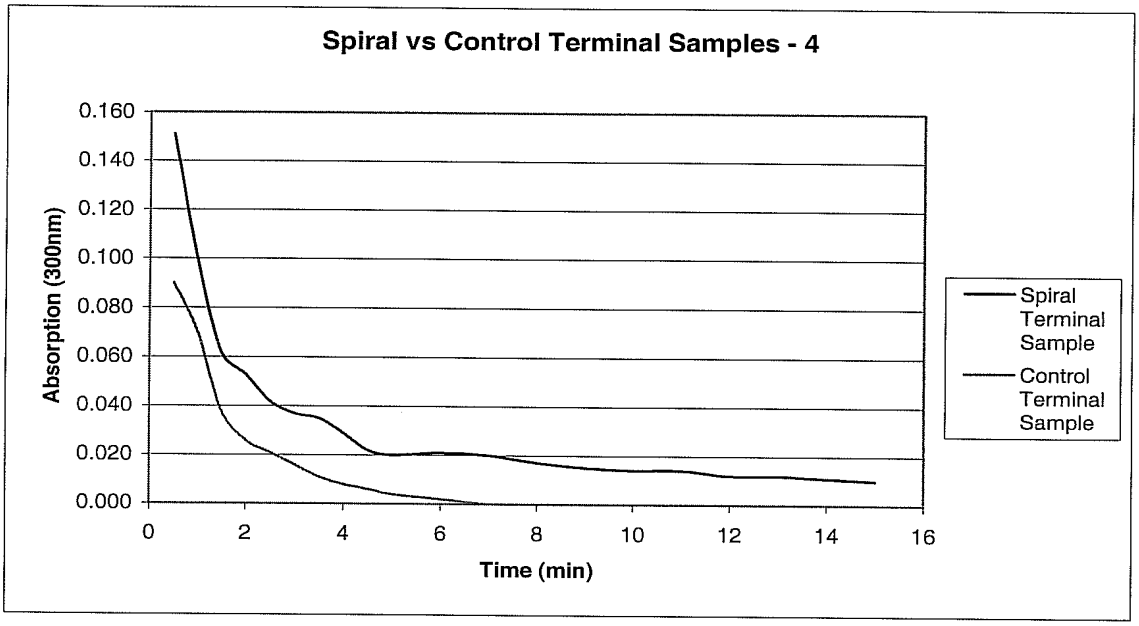
14. Fourth Run of Control vs Spiral

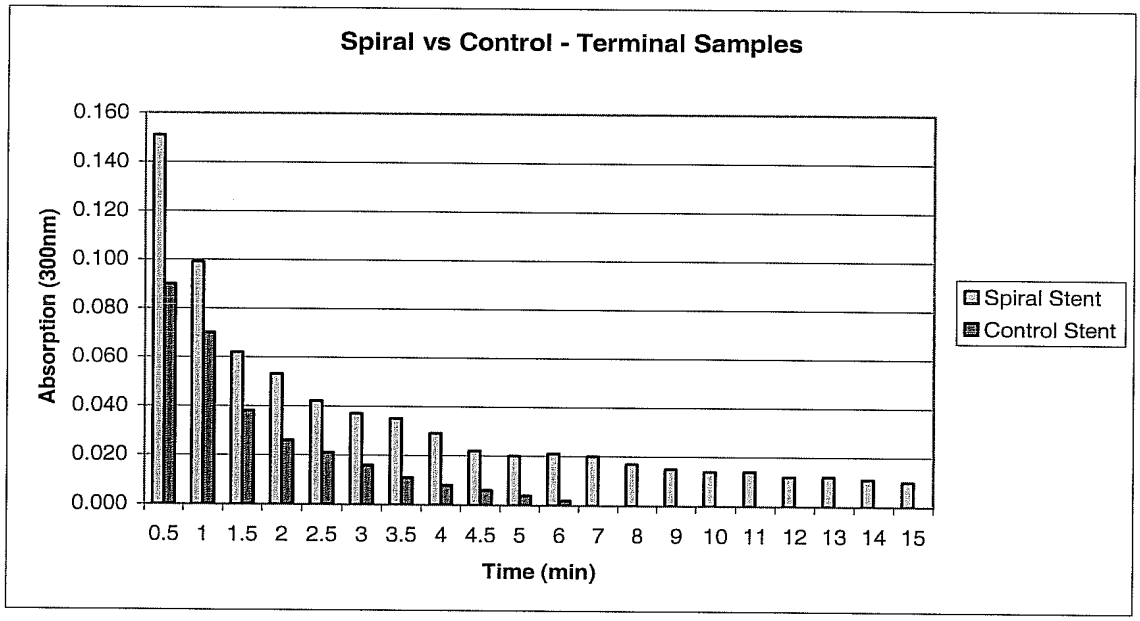
New stents were used for this run and a terminal sample was also taken to observe any differences in the results at a position further away from the stent.

The coating on the spiral stent weighed 50% more than the coating on the control.

The results obtained from the samples taken at the injection port begin as expected, with higher concentrations being released from the spiral stent, however at 4min the concentration of aspirin plummeted to reach zero within 2min. In order to discover what had happened the terminal samples were tested and showed (see below) that in fact, at that point, the absorption was exactly as expected i.e. the spiral stent had eluted 77.5% more aspirin than the control. The analyses of the data from the collection tank supported this, showing an 81% increase in the amount of aspirin eluted. It remains unclear what has caused this phenomenon.

Terminal Sample





15. Data Gathered from the Collection Tank

The data gathered from the collection tank shows that the spiral stents elute, on average (over 20 minutes), 71% more aspirin than the control stents. When using a calibration curve

to approximate the amount of aspirin eluted in each run, it became clear that in all four cases the spiral stent eluted far more aspirin than was even calculated to be present on the stent. The reason for this is unclear but one possibility is that the PU used to make the spiral binds aspirin tightly, or the aspirin crystals do not dissolve to form homogenous solution, thus the ratio of aspirin in the coating may be increased.

16. Preliminary Result using Control Stent

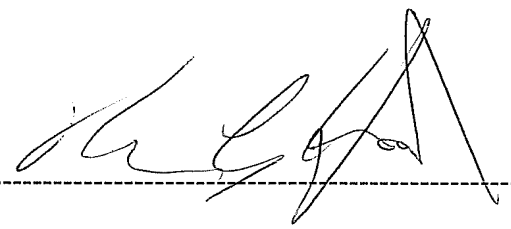
This experiment demonstrated that aspirin can be released from a stent, in measurable quantities 5 cm distal to the stent, in defined flow conditions. The release of aspirin from the stent appeared to fluctuate , represented by the peaks and troughs shown in the line graph. (Possibly due to turbulent flow induced by the high flowrate (750ml/min). Subsequent tests reduced the flow rate to ~300ml/min to give flow conditions that are closer to those found in humans – carotid artery flow = 300-350ml/min.

The amounts of aspirin eluted were extremely small, to obtain results that were more readily measured a higher dose of aspirin was added to the next coating mixture.

17. The data gathered shows the tested spiral modified stent is capable of 'holding' more coating than the control stent which is typical of normal stents. The tested spiral modified stent is capable of holding on average 56% more than those that are available on the market today.

The tested spiral stent eluted on average 71% more aspirin than the unmodified control stent.

Limitations to the study are discussed in Annex C.

Signed: 

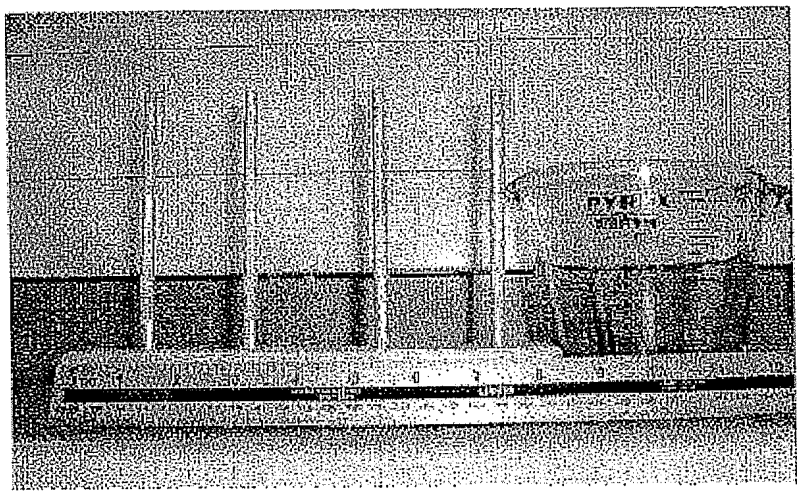
Dated: 27th October 08

ANNEX A

Described below is the protocol used to test the coating of stents with aspirin.

Coating Optimisation

Metal rods were used to determine the coating mixture with a suitable viscosity to coat the stents:



Experiment 1

1. Weigh out desired amount of toluene (adhering to COSHH guidelines)
2. Weigh out desired amount of Cronoflex polyurethane
3. Mix in a test tube
4. Apply coating by dipping rods into tube
5. Allow to cure overnight

Rods dipped in Cronoflex/Toluene Dispersions

	Rod 1	Rod 2	Rod 3	Rod 4
Dilution	50%	50%	100%	100%
Cronoflex (g)	10.5	10.5	7.5	7.5
Toluene (g)	5.25	5.25	7.5	7.5

The rods coated with equal amounts of cronoflex and toluene provided a uniform coverage.

Experiment 2 – Addition of Aspirin into the Coating

Follow steps 1-3 as above, add measured amount of aspirin, mix then coat rods as previous.

Rods dipped in Cronoflex/Toluene Dispersion with added Aspirin

	Rod 1	Rod 2	Rod 3	Rod 4
Dilution	100%	100%	200%	200%
Cronoflex (g)	5	5	5	5
Toluene (g)	5	5	10	10
Aspirin (g)	1	1	2	2

(Vacuum=17Kpa)

The addition of aspirin to the mix stopped the coating curing in the air. Rods were therefore placed in desiccator with silica beads overnight in a vacuum of 17 Kpa. This also proved unsuccessful in curing the coating. Therefore the rods were placed in an oven at 50°C until dry (30minutes).

Experiment 3 - Determine whether the Aspirin can be Eluted from the Coated Rods

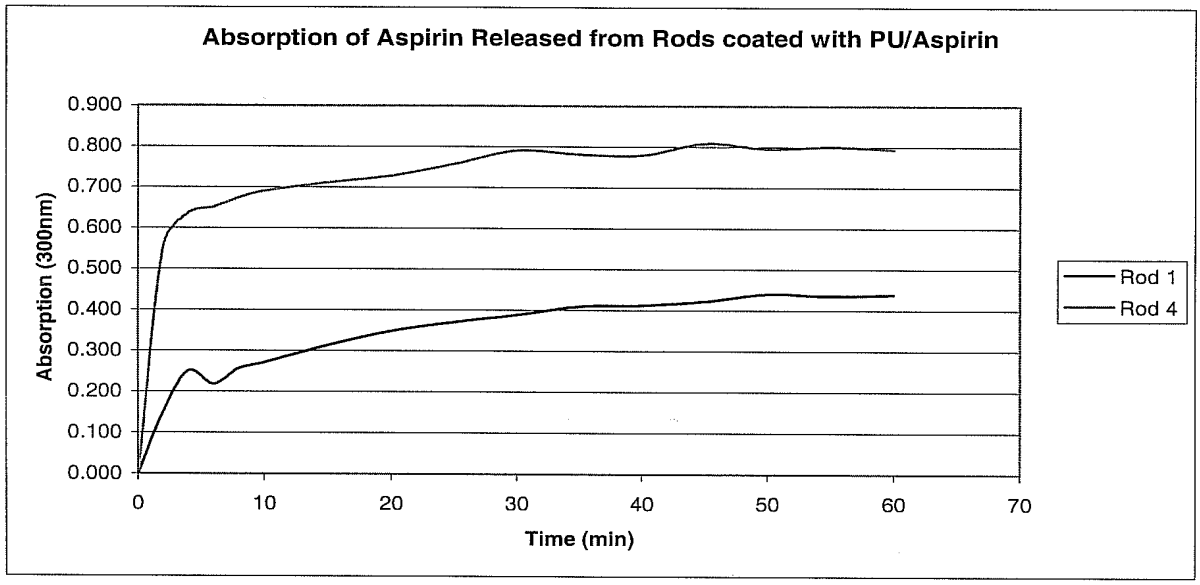
In order to test whether the aspirin can be eluted from the coating a "soak test" was carried out -

1. Fill a jug with 500ml water from the Millipore water system (CAL 012)
2. Add rod 1 to the water
3. Take 2ml of water from the jug every 2 minutes for a total of ten minutes
4. Thereafter a 2ml sample should be taken every 5 min for 50 min.
5. The samples are put into sample jars then sealed.
6. The samples are tested on a spectrophotometer at 300nm in order to ascertain the amount of aspirin being released into the water.

The above steps were also carried out using rod 4 with a slight change to step 3, samples were taken every minute for 10 minutes.

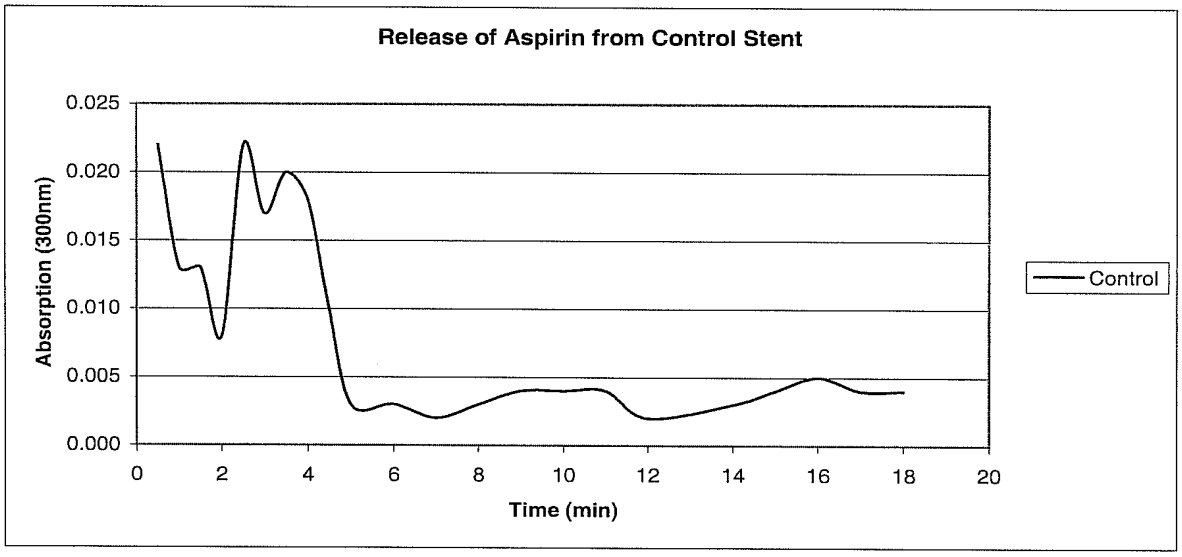
Results

Absorption of Aspirin Eluted from Coated Rods



Absorption of Aspirin from Stents

Preliminary Run using Control Stent – 2g Aspirin, 750ml/min



ANNEX B

The tests were carried out with the following configuration of coated stents.

A. Control stent was a coated standard plain stent in a 6mm tube.
B. Spiral stent was a coated stent of 6mm with a spiral inducer.

The spiral inducers had a P3 form (i.e. having a bell-shaped cross section) and a 20 degree spiral angle, and were also coated.

All test conditions as outlined, applied to both the control and spiral stents.

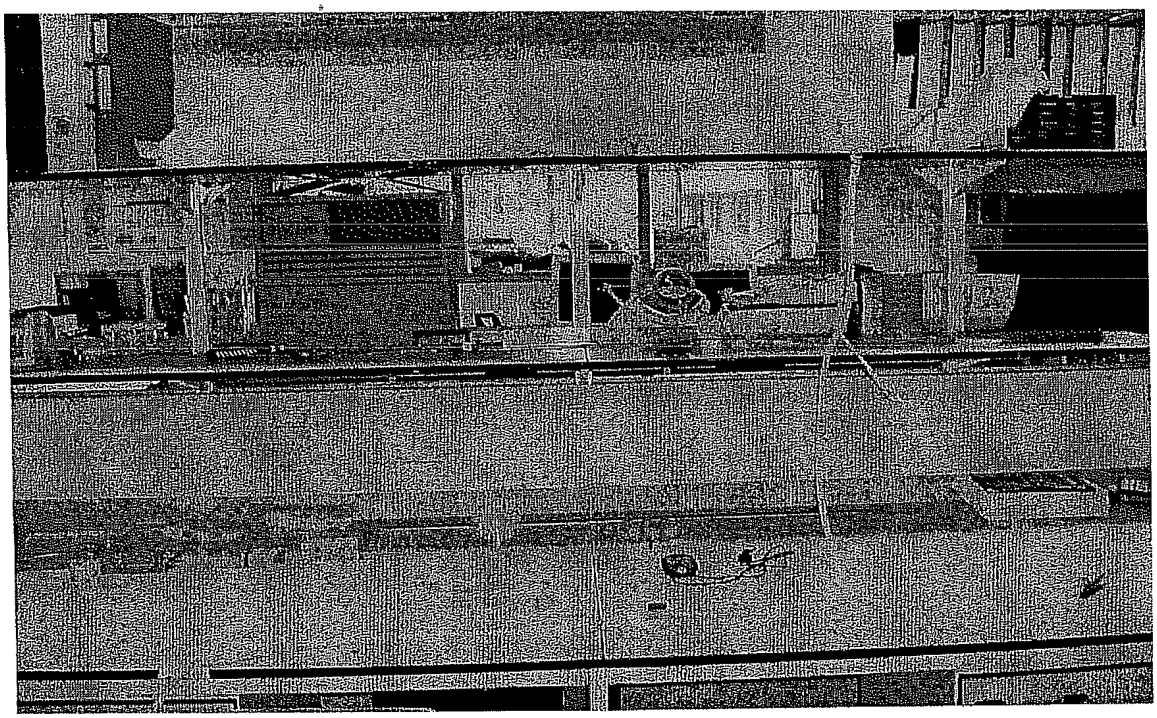
The protocol used to test the elution of drug from coated stents was as follows.

STENT COATING

The stents were dip coated in the same way as the rods as in Annex A but were allowed to drip dry in the air. The actual coating mixture for each stent is shown in Appendix 1.

Flow Rig Testing

The stents were tested in a flow rig, shown below:



The flow rig consists of:

- 20 litre tank with a tap to adjust flow rate
- 2.32m length of 6mm silicon tubing
- Injection port (blue)
- Collection tank (not seen)

Other equipment used:

- Surgical clamp
- Stopwatch
- Sample pots
- Syringe

Flow Rig Testing Methods

1. Fill tank up to a pre drawn mark with water from the Millipore water system (CAL012).
2. Attach tubing to the tap on the front of the tank, seal with silicon.
3. Cut tubing and insert injection port, seal with silicon.
4. Secure tubing into place on the bench with tape.
5. Position collection tank below the end of the tube.
6. Adjust tap to desired flow rate by measuring amount of water released per min. In this case ~300ml/min was appropriate to mimic carotid artery flow-rate
7. Clamp tube near to the tap.
8. Take a small sample of water from the tank to use as a blank when testing with the spectrophotometer.
9. Deploy coated stent at a position 5cm proximal to the injection port.
10. Release clamp to resume flow, start stopwatch.
11. Take a 2ml sample from the injection port every 30sec for 5min then every minute for a total of 15 or 20mins. Put samples into labelled sample pots.
12. In some cases a terminal sample may also be taken straight from the distal end of the tube at the same time intervals stated above.
13. Take a sample from the collection tank.
14. Samples can then be tested using a spectrophotometer.

Spectrophotometer Testing of Samples

Equipment used to test samples:

- Spectrophotometer
- 1.5ml quartz cuvette
- Syringe (without needle)

Method

1. Set spectrophotometer to measure absorption at 300nm.
2. Use syringe to transfer blank sample into the quartz cuvette.
3. Insert cuvette into the spectrophotometer and close lid. Zero the spectrophotometer.
4. Remove cuvette and exchange blank for the first sample to be tested. If the samples are tested in reverse order the cuvette does not need to be washed after every test. Insert sample into the spectrophotometer, close lid and record absorption given.
5. Repeat this process until all samples have been tested.

ANNEX C

Losses and Experimental Limitations

The experiments do not embed or encapsulate the aspirin, as such the measurements obtained from this experiment are not "controlled". It was impossible to ensure a homogenous mixture of PU, tolulene and aspirin with the equipment available. It is therefore reasonable to assume that the PU will have contained crystals of asprin, the release of these crystals is a possible explanation for the fluctuations in aspirin concentration that were apparent during many of the runs.

It is also possible that the spiral flow induced by the stent had an impact on the higher level of asprin eluted from the spiral stents. This hypothesis requires further study to determine the effect (if any) of spiral flow on drug elution in spiral stents.

Future Recommendations

This preliminary study shows a strong trend in favour of the tested spiral stent but in order to gather quantitative data that can be analysed statistically the following recommendations can be made.

- Obtain equipment i.e. Spectrophotometer, accurate balance, cuvettes etc. for the exclusive use of TFT. This would allow the tests to be carried out over longer runs, more often and when needed.
- Make appropriate number of stents to allow a fresh one to be used for every test, ensuring that the only difference between spiral and control stents was, in fact, the addition of the spiral and also that all spiral stents were identical, similarly for the controls.
- An automatic pump to regulate the flow rate. With the present set up the flow rate fluctuates throughout the test due to the change in pressure in the tank as the water level drops.
- Further development of the materials and methods to encapsulate the asprin (or drug of choice)

Appendix 1

First Run

Stents dipped in Chronoflex/toluene dispersion with added Aspirin

	Control Stent	Spiral Stent
Weight before coating (g)	0.17	0.27
Weight after coating (g)	0.21	0.36
Difference (g)	**0.04**	**0.09**
Dilution	200%	200%
Chronoflex (g)	5	5
Toluene (g)	10	10
Aspirin (g)	4	4

The coating on the spiral stent is 0.05g heavier than that on the control.

This is equal to a 55.5% increase in the spiral stent.

Second Run

Stents dipped in Chronoflex/toluene dispersion with added Aspirin

	Control Stent	Spiral Stent
Weight before coating (g)	0.15	0.30
Weight after coating (g)	0.19	0.40
Difference (g)	**0.04**	**0.1**
Dilution	200%	200%
Chronoflex (g)	5	5
Toluene (g)	10	10
Aspirin (g)	3	3

The coating on the spiral stent is 0.06g heavier than that on the control.

This is equal to a 60% increase in the spiral stent.

Third Run

Stents dipped in Chronoflex/toluene dispersion with added Aspirin

	Control Stent	Spiral Stent
Weight before coating (g)	0.16	0.32
Weight after coating (g)	0.22	0.42
Difference (g)	**0.04**	**0.1**
Dilution	200%	200%
Chronoflex (g)	5	5
Toluene (g)	10	10
Aspirin (g)	3	3

The coating on the spiral stent is 0.06g heavier than that on the control.

This is equal to a 60% increase in the spiral stent.

Fourth Run

Stents dipped in Chronoflex/toluene dispersion with added Aspirin

	Control Stent	Spiral Stent
Weight before coating (g)	0.20	0.34
Weight after coating (g)	0.22	0.38
Difference (g)	**0.02**	**0.04**
Dilution	200%	200%
Chronoflex (g)	5	5
Toluene (g)	10	10
Aspirin (g)	3	3

The coating on the spiral stent is 0.02g heavier than that on the control.

This is equal to a 50% increase in the spiral stent.

Appendix 2

Absorption of Aspirin Eluted from Coated Rods

	Absorption (300nm)	
Time (min)	Rod 1	Rod 4
0	0.000	0.000
2	0.150	0.555
4	0.250	0.636
6	0.218	0.651
8	0.256	0.674
10	0.271	0.690
15	0.313	0.711
20	0.348	0.728
25	0.370	0.757
30	0.388	0.790
35	0.409	0.781
40	0.412	0.779
45	0.422	0.808
50	0.440	0.795
55	0.435	0.800
60	0.438	0.793

Preliminary Run using Control Stent – 2g Aspirin, 750ml/min

Control Stent	
Time (min)	Absorption (300 nm)
0.5	0.022
1	0.013
1.5	0.013
2	0.008
2.5	0.022
3	0.017
3.5	0.020
4	0.018
4.5	0.010
5	0.003
6	0.003
7	0.002
8	0.003
9	0.004
10	0.004
11	0.004
12	0.002
14	0.003
15	0.004
16	0.005
17	0.004

Control Stent	
Time (min)	Absorption (300 nm)
18	0.004
19	0.028
20	0.025

First Run – 4g Aspirin, 280 ml/min

	Spiral	Control 1		
Time (min)	Absorption (300 nm)		Difference	% Increase in Absorption from Spiral
0.5	0.170	0.120	0.050	29.4
1	0.131	0.081	0.050	38.2
1.5	0.097	0.050	0.047	48.5
2	0.083	0.056	0.027	32.5
2.5	0.058	0.036	0.022	37.9
3	0.057	0.016	0.041	71.9
3.5	0.038	0.010	0.028	73.7
4	0.026	0.015	0.011	42.3
4.5	0.023	0	0.023	100.0
5	0.020	0	0.02	100.0
6	0.012	0	0.012	100.0
7	0.009	0	0.009	100.0
8	0.007	0	0.007	100.0
9	0.001	0	0.001	100.0
10	0.000	0	0	0.0
Average Increase in Absorption from Spiral (%)				**65.0**

Second Run – 3g Aspirin, 295ml/min

	Spiral	Control		
Time (min)	Absorption (300 nm)		Difference	% Increase in Absorption from Spiral
0.5	0.236	0.053	0.183	77.5
1	0.193	0.077	0.116	60.1
1.5	0.167	0.057	0.110	65.9
2	0.131	0.050	0.081	61.8
2.5	0.110	0.025	0.085	77.3
3	0.100	0.023	0.077	77.0
3.5	0.090	0.012	0.078	86.7
4	0.087	0.034	0.053	60.9
4.5	0.079	0.031	0.048	60.8
5	0.073	0.016	0.057	78.1
6	0.069	0.003	0.066	95.7
7	0.060	0.000	0.060	100.0
8	0.058	0.003	0.055	94.8
9	0.056	0.005	0.051	91.1

	Spiral	Control		
Time (min)	Absorption (300 nm)		Difference	% Increase in Absorption from Spiral
10	0.054	0.000	0.054	100.0
11	0.046	0.003	0.043	93.5
12	0.042	0.002	0.040	95.2
13	0.042	0.002	0.040	95.2
14	0.040	0.000	0.040	100.0
15	0.040	0.007	0.033	82.5
Average Increase in Absorption from Spiral (%)				**82.7**

Third Run – 3g Aspirin, 300ml/min

	Spiral	Control		
Time (min)	Absorption (300 nm)		Difference	% Increase in Absorption from Spiral
0.5	0.363	0.492	-0.129	-35.5
1	0.329	0.474	-0.145	-44.1
1.5	0.298	0.362	-0.064	-21.5
2	0.257	0.441	-0.184	-71.6
2.5	0.175	0.301	-0.126	-72.0
3	0.153	0.267	-0.114	-74.5
3.5	0.127	0.160	-0.033	-26.0
4	0.115	0.118	-0.003	-2.6
4.5	0.115	0.115	0.000	0.0
5	0.103	0.074	0.029	28.2
6	0.088	0.108	-0.020	-22.7
7	0.093	0.103	-0.010	-10.8
8	0.081	0.089	-0.008	-9.9
9	0.069	0.086	-0.017	-24.6
10	0.068	0.071	-0.003	-4.4
11	0.055	0.045	0.010	18.2
12	0.054	0.043	0.011	20.4
13	0.047	0.056	-0.009	-19.1
14	0.045	0.043	0.002	4.4
15	0.043	0.039	0.004	9.3
Average Increase in Absorption from Spiral (%)				**-17.9**

Fourth Run

Sample from Injection Port

	Spiral	Control	
Time (min)	Absorption (300 nm)		Difference
0.5	0.119	0.076	0.043
1	0.095	0.060	0.035
1.5	0.070	0.046	0.024
2	0.056	0.038	0.018

	Spiral	Control	
Time (min)	Absorption (300 nm)		Difference
2.5	0.035	0.027	0.008
3	0.033	0.025	0.008
3.5	0.026	0.022	0.004
4	0.007	0.020	-0.013
4.5	0.004	0.017	-0.013
5	0.002	0.016	-0.014
6	0.000	0.010	-0.010
7	0.000	0.009	-0.009
8	0.000	0.009	-0.009
9	0.000	0.007	-0.007
10	0.000	0.008	-0.008
11	0.000	0.007	-0.007
12	0.000	0.007	-0.007
13	0.000	0.006	-0.006
14	0.000	0.007	-0.007
15	0.000	0.002	-0.002

Terminal Sample

	Spiral	Control		
Time (min)	Absorption (300 nm) Terminal Samples		Difference	% Increase in Absorption from Spiral
0.5	0.151	0.090	0.061	40.4
1	0.099	0.070	0.029	29.3
1.5	0.062	0.038	0.024	38.7
2	0.053	0.026	0.027	50.9
2.5	0.042	0.021	0.021	50.0
3	0.037	0.016	0.021	56.8
3.5	0.035	0.011	0.024	68.6
4	0.029	0.008	0.021	72.4
4.5	0.022	0.006	0.016	72.7
5	0.020	0.004	0.016	80.0
6	0.021	0.002	0.019	90.5
7	0.020	0.000	0.020	100.0
8	0.017	0.000	0.017	100.0
9	0.015	0.000	0.015	100.0
10	0.014	0.000	0.014	100.0
11	0.014	0.000	0.014	100.0
12	0.012	0.000	0.012	100.0
13	0.012	0.000	0.012	100.0
14	0.011	0.000	0.011	100.0
15	0.010	0.000	0.010	100.0
Average Increase in Absorption from Spiral (%)				77.5

CURRICULUM VITAE (SYNOPSIS)

Personal Details

Full Name:	Robert Gordon Hood
Status:	Married, no children
Date of Birth:	04.04.1940
Nationality:	British
Home Address:	"Koinonia" 9 Rosamunde Pilcher Drive LONGFORGAN DD2 5EF Perth & Kinross

Professional Information

Awards and Recognitions:

Fellow of the Royal Society of Arts (FRSA) London

Fellow of the Institution of Engineering Designers (FIED)
(Formally Registered design Engineer [retired])

Diploma in Management Studies

Member, Plastics & Rubber Institute (MPRI)

Diploma in Polymer Technology, Napier University.

Positions Held (since 1982)

2000 –2006(retired)	Research & Development Director, Tayside Flow Technologies Limited
1999 – 2000	Consultant to: - Unipath plc, UK. Neoventa plc, Sweden. TFT Ltd etc. Scotland.
1993 – 1999	Managing Director / Technical Director, F.S.M. Technologies Limited Founder of FSM and Inventor of the technology
1993	Assisting in £5mil flotation of Tepnel Life Sciences plc
1992 – 1993	Director, Hood Consultancy
1987 – 1992	Director, Bioflo Limited Developed items of the Kelis Technology to commercial stage of Bioflo Ltd.

1984 – 1987	Director, Kelis Limited Founder and Inventor of a range of technology items for the biotechnology industry.
1984 – 1986	Executive, Health care and Biotechnology Division, Scottish Development Agency, and board representative of SDA to six companies.
1983 – 1984	Managing Director, Vascutek Limited Steered Vascutek to the market place via animal and clinical trials, and FDA 510K in the USA
1982 – 1983	Technical / Development Director, Vascutek Limited Inventor of the Vascutek vascular prosthesis systems for parent company (Coats Patons)

Past Honorary Positions

Research Fellow, Bioengineering Unit, Strathclyde University

Visiting Lecturer in Industry-related Biomedical Engineering, Post Graduate Medical School, Plymouth University.

Intellectual Property
(As Named Inventor.)

Membrane and Filtration based – seventeen patents

Systems Methodology – ten patents

Human Implants and Prosthetic Devices – twelve patents